

Endometriosis

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SUMMARY

The cause of endometriosis is not known. The incidence of the disease is greater than was previously suspected and it probably is increasing. Nulliparous women are more likely to have endometriosis than are women who have had children.

The commonest symptoms are lower abdominal pain, disturbance of menstruation, and dysmenorrhea, most often of the increasing or acquired type. Relative and absolute sterility are common partners of endometriosis.

A better percentage of correct preoperative diagnoses should be obtained in view of present knowledge.

Radical operation on women in the premenopausal age groups with endometriosis is resorted to in far too high a percentage of cases. The good results which can be attained with conservative therapy, including surgical and hormone therapy, should be stressed.

There is some evidence that endocrine therapy may control endometriosis. The dangers attending these methods have not as yet been determined.

THE purpose of this presentation is threefold: First, to emphasize the need of a continually thoughtful mind in diagnosing endometriosis. Second, to emphasize the importance of conservation of ovarian tissue in the premenopausal woman. Third, to review the problem as presented by a study of 153 patients operated upon in a small general hospital with a staff composed of specialists in obstetrics and gynecology, general surgeons and general practitioners.

There were 153 cases of proved endometriosis in this series taken from 2,660 cases of gynecological operations performed from January 1945 through January 1948. Thus the incidence was 5.7 per cent. This varies from some reports such as that of Meigs¹³ which was based upon private practice, but agrees essentially with the percentage he reported with regard to clinic patients and also with many other reports of similar studies. In the present study many cases had to be discarded because of lack of pathological confirmation, although the clinical description was classic. This point is important. Many times implants are not removed. It is the author's opinion, and one shared by many observers, that in the class of patients studied here the reported incidence in this series is far below the actual incidence.

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Endometriosis is definitely or seemingly increasing. Interest and knowledge are leading to more accurate diagnosis. Meigs¹³ reported with regard to patients treated by him in private practice that 35 per cent of those upon whom operation was done had endometriosis. As this percentage applies only to patients operated upon, many minor cases of this disease thus are not included. Fallon,⁴ reporting on observations of patients in a clinic, said that endometriosis was more common than acute appendicitis.

The incidence in the population at large is unknown, and because of pronounced variations between reports in the present literature, it is impossible to obtain a close estimate. In a recent article Beecham¹ reported the incidence of endometriosis in 1,000 consecutive gynecological office cases as 5.8 per cent.

The early symptoms of endometriosis are vague and in many cases a biopsy to make a positive diagnosis does not seem warranted. Thus the true incidence is unknown. Suffice it to say that the disease is more prevalent than was previously suspected.

In the present study the 153 cases were divided into the common classifications (as shown in Table 1):

1. Internal, or confined to the uterus—the so-called adenomyoma.
2. External, or found in the pelvis not involving the uterus.
3. Combined, involving both uterus and pelvic or other structures.

TABLE 1.—Incidence of Types of Endometriosis

Type	Number	Per Cent
Internal	60	39.2
External	83	54.3
Combined	10	6.5
Total	153	100.0

The incidence of the various classifications in various age brackets is shown in Table 2. The predominance of all cases lies in the age group from 30 to 55. In analyzing this table it is observed that adenomyosis occurs in a slightly older group of individuals than does external endometriosis. The incidence as reported here shows that the predominance of cases of internal endometriosis occurs in the age group from 35 to 55, while that of external endometriosis occurs in the group from 25 to 45. This confirms data noted by other observers.

In discussing statistics gathered in study of the 153 cases in the present report, an attempt will be made to elucidate the present-day opinions and views of writers relative to symptoms, signs, diagnoses, and treatment.

As revealed in the statistics of Table 3, there were

no specific symptoms of endometriosis. Ordinarily there was pain in the area involved, but even this was not constant. Dysmenorrhea was noted in 28.8 per cent of the patients in this series, as shown in Table 4. This was ordinarily of the increasing type. This figure corresponds well with that reported by Meigs¹³—26.4 per cent. Fallas and Rosenblum³ in a study of a similar nature reported an incidence of 43.4 per cent. The reported incidence of dysmenorrhea varies, depending upon the accuracy with which records are kept, but all observers record it as high. In the present series it will be noted that dysmenorrhea was more often associated with external than with internal endometriosis. This agrees with data reported by Fallas and Rosenblum and other observers.

Although dyspareunia is a symptom often associated with endometriosis, this is not revealed by the average record. It has been noted by the author

TABLE 2.—Age of Incidence by Type of Endometriosis

Age	TYPE OF DISEASE					
	INTERNAL		EXTERNAL		COMBINED	
	No. Cases	Per Cent	No. Cases	Per Cent	No. Cases	Per Cent
15-19..	0	0	0	0	0	0
20-24..	0	0	8	9.6	0	0
25-29..	1	1.7	11	13.3	0	0
30-34..	2	3.3	22	26.5	0	0
35-39..	13	21.7	16	19.3	3	30
40-44..	11	18.3	18	21.7	3	30
45-49..	15	25.0	7	8.4	1	10
50-54..	12	20.0	1	1.2	2	20
55-59..	4	6.7	0	0	1	10
60-64..	2	3.3	0	0	0	0
65-69..	0	0	0	0	0	0

TABLE 3.—Symptoms of Endometriosis

Complaint	Type of Disease			Total	Per Cent
	Internal	External	Combined		
Menorrhagia	23	16	4	43	28.1
Metrorrhagia	12	10	1	23	15.0
Polymenorrhea	0	1	0	1	.65
Uterine hemorrhage	2	0	2	4	2.6
Dysmenorrhea	13	31	0	44	28.8
Lower abdominal pain	13	47	6	66	43.1
Backache	15	10	2	27	17.7
Abdominal tumor					
(noted by patient)	2	7	1	10	6.5
Vaginal discharge	6	7	1	14	9.1
Bladder symptoms	10	2	0	12	7.8
Rectal pain	0	2	0	2	1.3
Menopausal bleeding	5	0	0	5	3.3
Gastrointestinal upsets	0	1	1	2	1.3
Dyspareunia	0	6	1	7	4.6
Sterility	3	10	0	13	8.5
General menopausal					
symptoms	6	3	1	10	6.5
Chronic abortion	0	1	0	1	.65
Pain in legs	3	1	0	4	2.6

TABLE 4.—Incidence of Dysmenorrhea in Endometriosis

Type	No. of Patients	No. with Dysmenorrhea	Per Cent
Internal	60	13	21.7
External	83	31	37.4
Combined	10	0	0
Total	153	44	28.8

and reported by others that close questioning of patients elicits information showing that the incidence is much higher than would be indicated in the perusal of hospital records. Endometrial nodules in the posterior cul-de-sac are most often painful to pressure.

Symptoms of bladder involvement are usually, as reported by Henriksen⁶ and McDougal and Deur,¹¹ frequency and dysuria occurring prior to the menses and continuing through it.

The other symptoms noted may be explained by associated pathological conditions in the particular organ involved, as shown in Table 5. Here it is noted that fibroids of the uterus occurred in 29.4 per cent of cases. Other observers have noted a somewhat higher incidence of this associated condition: Fallas and Rosenblum,³ 41.5 per cent; Novak¹⁴ 33.7 per cent. The most common associated pathological conditions were found in the ovary; the highest in incidence were simple follicular cysts—30.7 per cent. Thus, rather high incidence of endometrial hyperplasia might have been expected. The high incidence of associated pathologic change in the ovary undoubtedly partially explains the high percentage of irregular and profuse bleeding previously noted under symptomatology. Unfortunately, there was no specific report on the endometrium in most of these records. Novak and Alves de Lima¹⁴ recently reported a study relative to the incidence of changes in the ectopic endometrium as compared to the uterine endometrium. They reported endometrial hyperplasia in 23.4 per cent of the cases studied.

The high incidence of hyperplasia and perhaps anovulatory cycles may be a partial explanation of the relative sterility noted in patients with endometriosis.

In Table 6 the incidence of involvement of organs is shown, and the data agree in general with the findings in studies by others with regard to the average anatomical locations of endometriosis.

TABLE 5.—Associated Pathologic Conditions

	Type of Disease			Total	Per Cent
	Internal	External	Combined		
	Number of Cases				
Fibroid uterus	23	21	1	45	29.4
Ovarian disease:					
Simple follicular cysts	17	27	3	47	30.7
Lutein cysts	4	4	1	9	5.9
Multilocular cystadenoma	0	2	0	2	1.3
Hemorrhagic cysts					
(not chocolate)	6	10	1	17	11.1
Carcinoma ovary	0	0	1	1	.65
Dermoid cysts	1	0	0	1	.65
Fibromas ovary	0	1	0	1	.65
Chronic pelvic inflammatory					
disease	5	18	1	24	15.7
Endometrial hyperplasia	8	5	2	15	9.8
Chronic appendicitis	3	8	1	12	7.8
Acute appendicitis	1	0	1	2	1.3
Endometrial polyp	1	6	1	8	5.2
Cervical polyp	0	1	0	1	.65
Pregnancy, intra-uterine	1	0	0	1	.65
Carcinoma, body uterus	2	0	0	2	1.3
Uterus bicornis unicollis	0	2?	0	2	1.3
Chronic cervicitis	19	10	3	32	20.9
Endometritis	0	0	1	1	.65

There were no cases of the rare locations (such as arm, leg, or pleura) noted in the records of the 153 cases here reported upon.

DIAGNOSIS

The early diagnosis of endometriosis within the pelvis or abdominal cavity presents one of the most difficult problems in gynecology.

The history is particularly important, and awareness of the high incidence of the lesion should be borne in mind. Endometriosis usually produces pain of one kind or another. Dysmenorrhea of the acquired type is of particular importance. Pyrexia associated with pain occurring at the time of the menses is important. Jeffcoat⁹ demonstrated that in 10 per cent of patients observed by him pyrexia was an important factor in making the diagnosis. This occurs during the menses, the temperature not ordinarily going above 102° F., and disappearing one to two days after the flow ceases. This might possibly confuse the differential diagnosis in ruling out pelvic inflammatory disease.

Ovulatory charts thus become of dual importance. The incidence of anovulatory menstruation in adenomyosis is particularly high. Spatt¹⁵ reported 72 per cent in carefully studied cases.

The history of previous abdominal operations becomes of increasing importance in light of the high incidence of endometriosis, in this series, among patients who had had operations. As shown in Table 7, 49 per cent of the 153 patients in the series had undergone previous abdominal operations, and 33 per cent had had operation involving incision of the genital tissue. These figures are almost in exact accord with those from the Mayo Clinic presented by Counseller.²

In Table 8 it will be noted that in the present series 15.7 per cent of cases were correctly diagnosed preoperatively. This contrasts with 6.8 per cent reported (ten years ago) by Fallas and Rosenblum.³ Perhaps this is encouraging, as it would tend to show that gradually physicians are becoming more cognizant of this condition. There were, however, only 38.6 per cent diagnosed at the surgical table, which is about in line, in this respect, with the figures reported by Fallas and Rosenblum. Perhaps this indicates that surgeons are not looking for or are not familiar with the gross lesion of endometriosis.

At present there is no specific hormonal index or guide available in establishing or indicating the diagnosis. There are a few instrumental aids in the diagnosis of pelvic endometriosis, namely:

1. The vaginal speculum, which may show the typical dark-bluish dome cyst becoming visible through the mucous membrane.

2. The cystoscope, which is of aid in the diagnosis of vesical endometriosis.

3. The culdoscope, which Te Linde has shown to be a potent aid in the hands of a competent observer.

The proctoscope is of little aid in making a diagnosis of endometriosis involving the bowel.

TABLE 6.—*Involvement of Organs*

Organ	No. of Cases	Per Cent of Cases
Uterus	70	45.7
One ovary	63	41.2
Both ovaries	19	12.4
Pelvic peritoneum	27	17.8
Bladder	3	2.0
Sigmoid	7	4.6
Fallopian tube	5	3.3
Rectum	2	1.3
Small intestine	2	1.3
Round ligament	3	2.0
Uterosacral ligament	6	3.9
Cecum	1	.65
Infundibulopelvic ligament..	2	1.3
Umbilicus	1	.65
Cervix	1	.65
Broad ligament	8	5.2

TABLE 7.—*Previous Abdominal Operations*

Type	No. of Patients	No. with Previous Laparotomy	Per Cent	No. with Genitals Incised	Per Cent
Internal	60	37	61.6	27	45.0
External	83	35	42.2	23	27.7
Combined ..	10	3	30.0	1	10.0
Total ..	153	75	49.0	51	33.3

TABLE 8.—*Record of Diagnosis in 153 Cases of Endometriosis*

	No.	Per Cent
Diagnosed preoperatively	20	13.1
Suspected preoperatively	4	2.6
Diagnosed at operation	52	34.0
Suspected at operation	7	4.6
Diagnosis by pathologist only	70	45.8

The finding, on physical examination, of rather firm, irregular, nodular, and "shotty" feeling tissue behind the cervix, which is unusually sensitive, in conjunction with the history remains one of the best clues to pelvic endometriosis. The nodules in the uterosacral ligaments can usually be best identified by rectal-vaginal examination. Where the lesion is more extensive, involving the ovaries and broad ligaments, a similar nodular process may be felt, often in conjunction with fixation, and a small cystic tumor may be palpated.

Fixed retroversion of the uterus should always arouse suspicion of endometriosis. Due to the lack of notation in case records no accurate data relative to the position of the uterus and associated endometriosis could be obtained. This is a serious error and might have been a factor in the failures of diagnosis noted in this report.

Testosterone may be used as an aid in the presumptive diagnosis of endometriosis. It will often suppress the symptoms with alleviation of pain and many times cause temporary regression of the palpable nodules and cysts. The author uses this reaction in conjunction with the history, examination, and other factors, to establish a diagnosis.

The diagnosis, then, rests on: (1) Carefully taken history; (2) Adequate and careful pelvic examination; (3) Visualization wherever possible, and biopsy of tissue; (4) Suppression of symptoms when testosterone is given.

As the recognition of endometrial implants in the peritoneal cavity is familiar to anyone now doing abdominal and pelvic operations, this apparently is not a problem. What is important, however, is the necessity of searching for the smaller implants, biopsy if they are found, and destruction of them when possible. This must be stressed, for although endometriosis is not always an advancing disease, it is usually so in the presence of active ovarian tissue. As endometriosis usually develops slowly, recognition of it, with determination by biopsy, is important with regard to the patient's future.

Another symptom of endometriosis which alone brings the patient to the physician for examination is relative or absolute sterility. In this series the records indicated that this was the primary problem in only 26 cases or 16.9 per cent, but in many cases it was an incidental observation. Of 143 married patients, 69 had reproduced and 74 had not (Table 9). These statistics are in agreement with many reports; Counseller² noted almost the same division.

TREATMENT

Those physicians who are most cognizant of the problems involved in complete castration of the female are in accord on at least one phase of the subject—namely, that ovarian conservation is necessary wherever possible. This is emphasized by Beecham,¹ Meigs,¹³ Counseller² and others. Castration in the female should be given as much consideration as castration in the male. Every attempt should be made to conserve the vital function of the ovary and its influence on emotional and physio-

logical balance. In this series, as can readily be seen, this factor was not given that consideration. In this respect there is little variance in these statistics with those presented in many other studies of the past. However, this is no excuse for continuation of ill-considered castration in the reproductive age groups.

As shown in Table 10, radical operations were done in 34 per cent of the 153 cases in the present series, a far higher figure than is justified in the light of present knowledge. There was a high incidence of radical operation in patients of all the age groups (Table 11), and it was particularly high in the younger patients for whom the most conservative of operations would seem to be indicated. For patients past the average age of menopause, the retention of ovarian tissue is not of great importance, and in the presence of extensive endometriotic lesions, complete oophorectomy should be done.

It is impossible at present to determine rules of procedure in the treatment of endometriosis. Perhaps nowhere in medicine is the judgment of the physician more taxed in determining the right answer relative to the patient's future well-being. In the presence of certain specific lesions, the answer may be more specific, depending entirely on the extent of the lesion. Often more than one organ is involved. In determining procedure in a specific case, the following points must be considered:

1. The degree of endometriosis present and the organs involved.
2. The age of the patient.
3. The desires of the patient relative to pregnancy, and also in regard to production of an artificial menopause. Many women who are given a complete understanding will gladly risk future operation or intensive glandular therapy rather than have castration immediately.
4. The emotional status of the patient.
5. Severity of the symptoms.
6. The need for immediate exploration. Often the diagnosis is not exact and the physician may be suddenly confronted with signs of obstruction, hemorrhage, possibilities of acute appendicitis, rupture of a viscus, twisted pedicle cyst, etc. In such circumstances there may be no question about the need for immediate operation. However, all the above points

TABLE 9.—*Marital and Parity Status of Patients*

	Internal Only	External Only	Combined	Total
Married (parous)	34	31	4	69
Married (nulliparous)	25	44	5	74
Unmarried	1	8	1	10

TABLE 10.—*Type of Operation Employed*

Type	No. Cases	Conserv.	Per Cent	Radical	Per Cent
Internal	60	40	66.6	20	33.3
External	83	56	67.4	27	32.6
Combined ..	10	5	50.0	5	50.0
Total.....	153	101	66.0	52	33.9

TABLE 11.—*Operations in the Various Age Groups*

Age	Internal		External		Combined		Total			
	Conserv.	Radical	Conserv.	Radical	Conserv.	Radical	Conserv.	Per Cent	Rad.	Per Cent
20-24.....	0	0	6	1	0	0	6	85.7	1	14.3
25-29.....	0	1	13	0	0	0	13	92.8	1	7.2
30-34.....	0	1	16	6	0	0	16	69.6	7	30.4
35-39.....	10	4	11	4	0	3	21	65.6	11	34.4
40-44.....	9	2	8	11	3	0	20	60.6	13	39.4
45-49.....	9	6	1	5	1	0	11	50.0	11	50.0
50-54.....	10	2	1	0	1	1	12	80.0	3	20.0
55-59.....	1	3	0	0	0	1	1	20.0	4	80.0
60-64.....	1	1	0	0	0	0	1	50.0	1	50.0
Total.....	40	20	56	27	5	5	101	66.0	52	34.0

must be kept in mind when the actual lesion is determined to be endometriosis.

Simple endometrial cysts of the ovary often can be shelled out easily and the major portion of the functioning ovary preserved. This is done routinely by many physicians, including the author. It is no guarantee against further growth, but in many cases it is in itself sufficient.

Adenomyosis in women near the menopause is best treated by hysterectomy. In younger women, unless the lesion is of major extent, presacral sympathectomy will most often relieve severe dysmenorrhea. Presacral sympathectomy is of little value in endometriosis of the combined type, particularly if the pain is ovarian. If the infundibulopelvic ligament is resected, it may relieve ovarian pain but the blood supply of the ovary is seriously affected. If retroversion of the uterus is present in younger women, it is advisable to suspend the uterus in view of the high incidence of fixation and pain, dyspareunia, and further extension of the process into the rectovaginal septum.

Serious lesions of the bowel produced by endometriosis are not common. McGuff, Dockerty, Waugh and Randall¹² observed only 16 cases producing obstruction in 20 years' experience at the Mayo Clinic. In the present series, there were 12 cases involving the bowel, an incidence of 7.85 per cent. However, in none of these cases was the bowel obstructed. If symptoms of bowel obstruction arise, however, any patient regardless of age should be operated upon as soon as practicable. The type of operation depends on factors of age, involvement, and location of the lesion.

A phenomenon which has made a tremendous impression on the author is the regression of endometriosis during pregnancy. This has been observed by the author in every carefully followed case in his own practice, and it has been noted by other observers. In many of these cases there has been little regrowth, but in time the transplants ordinarily become reactivated unless further pregnancy intervenes. There is a tremendous bombardment of the endometrial implants by estrogen during this physiological amenorrhea which seems to have a depressing effect on the growth of the aberrant tissue.

In an attempt to produce a long period of amenorrhea, Karnaky¹⁰ has been treating patients with increasingly potent doses of diethyl stilbestrol. By this means, patients have been kept relatively amenorrheic for a period of several months. Karnaky reported almost complete regression of endometrial transplants in all patients so treated. This sounds feasible in view of the physiological results often associated with pregnancy, and if it is borne out in further experience it offers hope such as no other method to date can equal. Thus far the author has not had sufficient experience with this method to draw a conclusion, but patients being treated by this method are now under observation.

Hurxthall and Arnold⁷ reported that three patients with endometriosis were treated successfully with moderately large doses of diethyl stilbestrol.

They believed the basis of relief was suppression of progesterone. Misgivings were expressed regarding the long-term effect of estrogenic stimulation over a long period. Two of the patients were reported on after 18 and 24 months of continuous diethyl stilbestrol therapy.⁸ Endometrial biopsies indicated endometrium of hypoplastic type. As a result of these reports, this method of approach to the problem of endometriosis bears intensive study.

The use of testosterone in many cases offers a real aid in controlling the regrowth of ectopic endometrium following conservative operation. It should be kept in the armamentarium of the physician for use when necessary. Testosterone should also be kept in mind for use in controlling the symptoms of artificial menopause in younger patients who have been subjected to radical operation with castration and attending sequelae.

Greenblatt⁵ reported very successful results in experience with pellet implantations of testosterone, intramuscular testosterone propionate and methyl testosterone by mouth in the treatment of endometriosis. The author has had no experience with pellet implantations, but oral and intramuscular use has often given dramatic relief.

No trials of hormone therapy were reported in the case records of the patients studied in this series.

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